REMARKS

Claims 10-13, 18 and 23-39 are pending in the present application. By virtue of this response, claims 10, 18, 27, and 38 have been amended, claims 23-25, 35 and 36 have been canceled, and new claims 40, 41, and 42 have been added. Accordingly, claims 10-13, 18, 26-34, 37-39 and 40-42 are currently under consideration.

By this amendment, independent claims are amended to recite "c-myc," which is previously found in dependent claims 25 and 36. Support for the amendments of claims 10, 18, 27 and 38 can be further found, for example, on page 18, first paragraph and, for example, on page 21, last paragraph of the specification. Support for new claims 40-42 can be found, for example, on page 23, second last paragraph to page 24, first paragraph of the specification, and in claims 29-31. No new matter has been added.

With respect to the cancellation and amendment of claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover, have not acquiesced to any rejections and/or objections made by the Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation, continuation-in-part, and/or divisional applications.

Interview Summary

Applicants thank Examiner Catherine Hibbert for the courtesy in conducting a telephonic interview with Applicants' representative Jian Xiao on December 6, 2011. Applicants' representative and the Examiner discussed possible claim amendments to further prosecution. The Examiner discussed that the Applicant may submit the proposed claim amendments in an after-final amendments and that the Examiner would consider whether the proposed claim amendments would be entered. The present claim amendments reflect the proposed claim amendments discussed at the interview. The guidance provided by the Examiner during the interview is greatly appreciated.

Response to Amendments/Arguments

Applicants acknowledge with thanks that the Examiner has withdrawn the objection to the specification in view of the amendment to the specification filed 6/24/2011. Applicants acknowledge with thanks that the Examiner has withdrawn the rejection of claims 23-25 and 35-36 under 35 U.S.C. §112, second paragraph based on claim amendments filed 6/24/2011.

Claim Rejections – 35 USC § 103

Claims 10-13, 18 and 23-39 stand rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Zubiaga et al. ("Zubiaga", Molecular Cell Biology 1995, Vol 15, No. 4, pages 2219-2230), in view of Banholzer et al. ("Banholzer", Molecular Cellular Biology, 1997, Vol 17, No. 6, pages 3254-3260), further in view of Lemm and Ross ("Lemm and Ross", Molecular and Cellular Biology, 2002, Vol 22, No. 12, pages 3959-3969).

Solely to expedite prosecution and without acquiescing to this rejection, claims 10 and 18, from which claims 11-13, 26-34, 37-39 and new claims 40-42 depend have been amended to recite " a heterologous instability sequence from c-myc." Claims 23-25 and 35-36 have been canceled. Applicants submit that Zubiaga, Banholzer and/or Lemm and Ross alone or in combination, do not render amended claims 10 and 18 and their dependent claims obvious.

Amended claims 10 and 18 and their dependent claims are directed to methods of screening/high throughput methods of screening using a DNA expression system, wherein the mRNA which is transcribed from said expression system comprises at least one copy of a heterologous mRNA instability sequence comprising one or more coding region determinant (CRD) of c-myc or a fragment thereof comprising at least eight contiguous nucleotides.

The Examiner cites Lemm and Ross as allegedly teaching that a 249 nucleotide coding region from c-myc destabilizes c-myc and that such sequence destabilizes β-globin mRNA when inserted in frame within the coding region of β-globin. The Examiner thus states that "it would have been obvious to one of ordinary skill in the art to use the cell lines with constructs that have instability sequence as taught by either Zubiaga. or Banholzer to test compounds that affect coding region instability determinants (CDR) from c-myc." Page 8 of Office Action. Applicants respectfully disagree.

Lemm and Ross teach that c-myc contains an instability determinant in its coding region which modifies mRNA half-life in a translation-dependent manner. Page 3959, left column, second paragraph. This c-myc coding region instability determinant (CRD) functions independently of the AU-rich element to make the mRNA instable. Page 3959, right column, second paragraph. Notably, Lemm and Ross teach that the c-myc CRD "must be translated to destabilize the mRNA," and that "[p]lacing a translational stop codon upstream of the CRD stabilizes the chimeric RNA." Page 3959, right column, second paragraph. Lemm and Ross further discuss that "ribosomes pause within the 5' segment of the CRD." According to Lemm and

Ross this "translational pausing" accounts for their observations that "CRD-containing mRNAs are translated relatively inefficiently", and that "CRD mutations that increase translational efficiency and reduce ribosome pausing *in vitro* also lead to increased mRNA stability in cells." Page 3965, right column, third and fourth paragraph.

One of ordinary skill in the art reading Lemm and Ross would thus clearly understand that the function of the CRD discussed therein requires translation of the CRD sequence. In other words, the CRD has to be present in the coding region in order for "translational pausing" to occur, and that placing the CRD into the 3'UTR (*i.e.,* after a stop codon) would be ineffective in destabilizing mRNA. This was also acknowledged by the Examiner in the previous Office Action, which states that the 249 nucleotide coding region from c-myc "destabilizes beta-globin mRNA when inserted in frame within the coding region of said beta-globin gene." Page 9 of Office Action dated 3/24/2011.

Based on the teachings of Lemm and Ross that the CRD of c-myc has to be inserted in the coding region to destabilize the target mRNA, the skilled artisan would have had no motivation to combine Lemm and Ross with either Zubiaga or Banholzer Specifically Zubiaga focuses on identifying the minimal AU-rich motif capable of destabilizing mRNA. Various constructs comprising different ARE sequences inserted into the 3'UTR of the β-globin gene were made and transiently transfected into NIH 3T3 cells. Since Lemm and Ross teach to insert c-myc CRD into the coding region, a skilled person would not use the cell lines and constructs taught by Zubiaga to test compounds that affect coding region instability determinants (CDR) from c-myc.

Banholzer focuses on understanding the mechanisms by which rapamycin ("RAPA"), a known immunosuppressive drug, downregulates IL-3 mRNA in a tumor mast cell line. Genomic IL-3 wild-type sequences or a sequence lacking the AU-rich element (ARE) in their 3'UTR were transfected into separate tumor cell lines. The effects of rapamycin on the IL-3 mRNAs were evaluated. To determine whether the 3'UTR of IL-3 would confer sensitivity to a heterologous transcript, Banholzer also examined the effect of rapamycin on AP reporter constructs carrying the 3'UTR of IL-3 with or without deletion of the ARE. Since also Banholzer teaches only constructs and cell lines carrying instability sequences in the 3'UTR, the skilled artisan would not be motivated to use these cell lines and constructs to test compounds that affect coding region instability determinants (CDR) from c-myc.

Furthermore, Banholzer concluded that "IL-3 3'UTR could confer RAPA sensitivity to reporter transcripts, provided that the 3'UTR sequence was intact." Banholzer thus conveys to a person of ordinary skill in the art that, for the purpose of studying the effect of rapamycin and/or other compounds on IL-3 mRNA, it is important to keep the mRNA instability sequence in its natural state. Thus, a skilled artisan would not be motivated to apply the teachings of Zubiaga to insert heterologous instability sequences into the 3'UTR of another gene to the teachings of Banholzer which emphasizes that an intact 3'UTR sequence is needed in order to confer sensitivity to the tested compounds. Neither Banholzer nor Zubiaga teaches a CRD sequence from c-myc. Thus, even if one were motivated to combine the teachings of Banholzer and Zubiaga., such combination would not lead the skilled person to arrive at the method claimed in the present application. This is especially true in view of the teaching in Lemm and Ross that the c-myc CRD is translation dependent.

In summary, Applicants respectfully submit that Lemm and Ross not only provide no motivation but rather teach away from inserting a CRD from c-myc into an heterologous 3'UTR construct of Zubiaga, which is designed to identify the minimal AU rich sequence motif that destabilizes mRNA or from inserting a CRD from c-myc into the 3'UTR of IL-3 in a construct disclosed by Banholzer which is designed to test the effect of rapamycin on the 3'UTR of IL-3 and requires an intact 3'UTR.

In response to Applicants' arguments presented in the response filed on 06/24/2011, the Examiner cites Davis et al. (JCB, October 2001, Vol 276, No 40, pages 37317-37326), which allegedly teach insertion of a CRD of Manganese Superoxide Dismutase into a 3'UTR. Applicants submit that Davis et al. do not teach or suggest an expression construct comprising a heterologous instability sequence from c-myc as currently claimed. As discussed above, given the teaching of Lemm and Ross that the c-myc CRD requires translation of the CRD sequence, the skilled artisan would not be motivated to combine Lemm and Ross with Banholzer and/or Zubiaga.

In view of the above, Applicants respectfully submit that the cited references do not render amended claims 10 and 18 and their dependent claims obvious. In view of the foregoing, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. §103.

Double Patenting

Claims 10-13, 18 and 23-29 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 10-14, 18, 23-25, 27-32, and 34-43 of copending Application No. 11/868,397 (US2009/068654).

Applicants respectfully traverse. However, Applicants note the provisional nature of this rejection and will address it at the appropriate time in the appropriate application, *e.g.*, upon indication that the claims are otherwise allowable.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

CONCLUSION

If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing **docket no. 608352000101**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: January 12, 2012

Respectfully submitted,

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